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Influenza in Canada during 1949*

INCLUDING STUDIES ON ESKIMOS

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A study of influenza epidemics occurring in the Dominion during 1948-9 has been sponsored by a grant from the Defence Research Board of Canada. Following arrangements made with Mr. J. Gibbard, Director of the Laboratory of Hygiene, Department of National Health and Welfare, Ottawa, and Dr. R. P. Hardman, Epidemiologist of the Provincial Department of Health, Toronto, nose and throat washings as well as sera were obtained from patients in a series of outbreaks throughout the Dominion during February and March of 1949. Material was also obtained from service personnel through the co-operation of Lt.-Col. R. J. Nodwell, R.C.A.M.C., Central Command, Oakville, Ontario. The object of the investigation was to conduct a comprehensive study of the type incidence of influenza virus responsible for illness during the winter season. Investigations of specimens submitted from the Northwest Territories was possible through the assistance of Dr. P. E. Moore, Department of Indian Affairs, Ottawa.

Clinical Features

Both sexes of all ages were affected. Clinical data of some 40 cases showed that the disease was mild in character and patients were usually not confined to bed for more than three to four days. No deaths were reported, except from the more serious outbreak in the N.W.T.

The clinical signs and symptoms were those of febrile catarrh, ushered in by headache, generalized aches and pains, weakness, fever ranging from 99 to 105°F., accompanied by dry cough, rhinitis and occasionally physical signs of

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pneumonia. In a few cases, the leucocyte count was 6 to 7000 W.B.C. in the early stages of the illness.

Methods

Broth-saline throat washings were gathered from patients, frozen in CO_2 dry ice, packed in insulated containers and transported by air to the laboratory. Post-mortem material was handled likewise; serum was sent unfrozen. Before use, material was thawed and to this was added 1000 units per ml of penicillin and streptomycin. Thereafter 13-day-old embryonated eggs were inoculated in the amniotic sac with a No. 22 gauge 1½-inch needle. After three days' incubation at 96.5°F. amniotic fluid was harvested and tested for presence of haemagglutinins for fowl and guinea-pig erythrocytes.

Positive samples were pooled and further subinoculated in 11-day-old embryonated eggs via the allantoic sac route. Negative samples were pooled and again passaged by the amniotic route.

In all instances when virus was recovered it was obtained after not more

TABLE I

SUMMARY OF VIRUS ISOLATIONS FROM NOSE AND THROAT WASHINGS

Location of Epidemic	Date of Collection of Specimens	Physician Submitting Specimen	No. of Specimens	No of Isolations	Type
Sault Ste. Marie, Ontario	Feb. 9	Dr. J. Bell, Ont. Dept. of Health	10	3	Unidentified (?) A-prime
Montreal, P.Q.	Mar. 2	Dr. R. Cyr, Ministry of Health, P.Q.	2	9	No virus isolated
St. Catharines, Ontario	Mar. 7	Dr. D. V. Currey M.O.H., St. Catharines	7	6	Unidentified (?) A-prime
Chorley Park Military Hospital, Toronto	Mar. 9-17	Maj. R. D. Appleford, R.C.A.M.C.	14	19	Unidentified (?) A-prime
Edmonton, Alta., Military Hospital	Mar. 21-26	Dr. R. M. Shaw, Provincial Lab., Edmonton	7	2	Unidentified (?) A-prime
Cobourg, Ontario	Mar. 22	Dr. J. Bell, Ont. Dept. of Health	4	3	Unidentified (?) A-prime
Saint John, N.B. Military Hospital	Mar. 26	Dr. A. Branch, Lancaster Hosp., Saint John	5	5	Unidentified (?) A-prime
Regina, Sask.	Apr. 20	Dr. W. A. Riddell, Dept. of Pub. Health, Regina	2	2	A
Newmarket, Ont.	May 2	Dr. J. Bell, Ont. Dept. of Health	7	1	Unidentified (?) A-prime

than two transfers, and in approximately one-third of the cases, after the first amniotic inoculation. Material yielding a negative response after the second amniotic egg passage was discarded.

Each strain isolated was subsequently grown in allantoic fluid and tested for evidence of haemagglutination inhibition by specific rabbit A (PR8) and B (Francis) antiserum. The latter was performed employing the method of Miller and Stanley (1944), the results being read with the aid of a Klett Summerson photo-electric colorimeter.

Results

Nine epidemics appearing in different parts of Canada, exclusive of the N.W.T., have been investigated. Table I contains a list of these arranged in chronological sequence of notification of illness, with place of occurrence and other data.

As will be observed from Table I, a total of 32 strains of influenza virus was isolated from 58 nose and throat washings submitted.

Typing Tests

Reviewing the results collectively, it could be stated that only in two instances was it possible to identify the virus with certainty. Thus, two strains of typical A virus were recovered from Saskatchewan on April 20th. In the case of the remaining 30 strains, difficulty was experienced in typing. Despite efforts at direct typing of the virus, as well as attempts to find the serological antibody response, it has not been possible to assign these strains to category A or B. Furthermore, in our series there was little or no response shown by the patients' serum against the homologous infecting virus.

Twenty-nine of these strains were forwarded for opinion to Dr. T. P. Magill at the U.S. National Influenza Strain Study Center, Long Island Medical College, New York. Dr. Magill reported that they were more closely related to A than B and suggested that they be tentatively designated group A-prime (FM1). The latter strain of influenza virus has been described by Sigel *et al* (1948).

More recently, Francis, Quilligan and Minuse (1949) revealed that the Oti strain of influenza virus isolated in 1939 from endemic swine influenza in Korea, was antigenically related to the A-prime group responsible for human cases in 1947.

Canadian Arctic Epidemic of 1949

During the latter half of April 1949 an epidemic of upper respiratory illness occurred at Cambridge Bay, on Victoria Island, situated within the Arctic Circle of the Canadian North West Territories. Following notification of the outbreak, Dr. P. Moore, Department of Indian Affairs, and Mr. J. Gibbard, Director of the Dominion Laboratory of Hygiene, Ottawa, made arrangements for the collection of specimens. Dr. F. P. Nagler, of the Dominion Laboratory of Hygiene, accompanied by Dr. J. H. Sturdy, Pathologist of the Royal Alexandra Hospital, Edmonton, travelled by air to the affected area.

On arrival, it was learned that of a population of some 90 Eskimo inhabitants of this island, 17 had died and 50 were admitted to hospital with influenza. Post-mortem tissue was obtained from 3 subjects and throat washings were procured from 12 patients and the material transmitted by air to the Connaught Medical Research Laboratories, Toronto.

TABLE II

SUMMARY OF VIRUS ISOLATIONS AND TYPING OF NEW STRAINS

Patient	Material	Virus Designated	Virus + specific immune serum		
			PR8 immune	Lee immune	Normal
Ban	Throat washings	Canadian Arctic No. 1A	2048	32	32
Wil	" "	Canadian Arctic No. 2A	2048	32	32
Hatk	" "	Canadian Arctic No. 3A	1580	32	32
Ekh	" "	Canadian Arctic No. 4A	1820	45	32
Gwe	" "	Canadian Arctic No. 5A	2048	32	32
Hat	" "	Canadian Arctic No. 6A	2048	32	32
Aop	" "	Canadian Arctic No. 7A	2048	32	32
Kin	" "	Canadian Arctic No. 8A	1480	53	64
Too	" "	Canadian Arctic No. 9A	2048	32	32
Avi	" "	Canadian Arctic No. 10A	1680	32	32
Car	" "	Canadian Arctic No. 11A	2048	32	32
Meg	Lung tissue (post-mortem specimen)	Canadian Arctic No. 12A	1290	32	32

Figures show reciprocals of dilutions of specific immune serum which inhibit 50 per cent agglutination of RBC in presence of 4 agglutinating units of virus.

Following egg inoculation, virus was recovered after the second amniotic passage in 11 out of 12 instances from throat washings; and from 1 out of 3 post-mortem specimens of lung. Positive results were also obtained from the latter human tissue after the second mouse passage. Preliminary results suggested that all strains recovered from the outbreak showed specific high titre activity against Type A (PR8 strain) immune serum.

A summary of serological findings and isolation results is contained in Tables II and III.

TABLE III

SUMMARY OF SEROLOGICAL FINDINGS

Patient's Name Abbreviated	Date of Admission to Hospital	Date of Collection of serum	Antibodies to PR8 strain A	Antibodies to Lee strain B	Antibodies to Arctic virus
Sam		27.4 12.5	684 457	64 64	851 624
Aka	21.4	27.4 12.5	151 512	128 90	380 760
Hat	21.4	27.4 12.5	64 64	64 64	64 64
Dom	20.4	27.4 12.5	64 64	64 64	64 64
Too	23.4	27.4	204	158	91
Kim	21.4	27.4	70	77	64
Gwen		27.4	871	64	512
Con	29.4	30.4	684	109	355

Figures show reciprocals of serum-dilution which inhibits 50 per cent agglutination in presence of 4 agglutinating units of virus.

SURVEY OF NEUTRALIZING ANTIBODIES

Through the courtesy of Dr. Malcolm Brown, Queen's University, Kingston, 120 sera were obtained from adult Eskimos at Southampton Island following an expedition to this area in September, 1947. The results of neutralizing tests provide a basis for comparison with the antibody level of a similar adult group of 92 sera derived from Toronto University personnel. In September 1949 another series of sera submitted by Dr. Malcolm Brown was gathered from a group of Eskimos as far north as Igloolik, where contact with the white man is very infrequent.

TABLE IV

A ANTIBODY-LEVEL

Place of Collection	Number of sera	Reciprocals of serum-dilutions						
		<32	32 to 64	64 to 128	128 to 256	256 to 512	512 to 1024	1024 to 2048
Toronto sera (percentage showing neutralizing antibodies in various dilutions)	92	25%	21.7	28.2	14.1	9.6		1 case
Southampton Island Eskimo sera (1947)	120	97.5%	2.5					
Igloolik Eskimo sera (1949)	104	97.11%	1.92	0.97				

B ANTIBODY-LEVEL

Place of Collection	Number of sera	Reciprocals of serum-dilutions						
		<32	32 to 64	64 to 128	128 to 256	256 to 512	512 to 1024	1024 to 2048
Toronto sera (percentage showing neutralizing anti-	92	19.5%	52.1	22.8	4.3	1 case		
Southampton Island Eskimo sera (1947)	120	65%	33.3	1 case	1 case			
Igloolik Eskimo sera (1949)	104	79.8%	17.3	2.9				

Southampton Island and Victoria Island are about 500 miles apart, but both are lonely outposts of humanity and the total Eskimo population of Victoria Island numbers about 90 persons. It is probable that sera gathered from Southampton Island in 1947 were representative specimens indicative of the prevailing low level of antibodies to influenza virus among the local Arctic inhabitants. More data was obtained on sera from Igloolik, a small island located at the north-eastern tip of Melville Peninsula situated at approximately latitude 69 and longitude 82 degrees. Dr. Malcolm Brown has infomed us that the inhabitants comprise a group of some 300 Eskimos of a type more primitive than other denizens of the Eastern Arctic.

The results reveal the low natural antibody level in adult Eskimos in comparison with the city population of Toronto.

PATHOGENICITY TESTS

Mice were anaesthetized with ether and 0.05 ml of infected allantoic fluid was introduced intranasally. The results are summarized in Table V and it will be noticed that there was considerable difference in the virulence of individual strains. Thus, all strains recovered from the Cambridge Bay epidemic, designated Canadian Arctic Nos. 1 to 12, invariably produced death and pulmonary consolidation after three to eight days. With two exceptions, virus isolated from clinically mild cases occurring throughout the Dominion earlier in the winter were relatively non-pathogenic.

Similar results were obtained following intraperitoneal inoculation of the same infected allantoic fluid.

ELECTRON MICROSCOPY

Two strains of virus cultivated in allantoic fluid were deposited by centrifugation at 11,000 r.p.m. on an angle centrifuge, and the deposited virus repeatedly washed by differential centrifugation in saline. Electron microscope mounts were made after the usual manner, shadowcast with chromium metal and thereafter photographed.

TABLE V

Strain	Number of Allantoic Passages	Intranasal inoc. 0.05 ml			Intraperitoneal inoc. 0.5 ml.		
		Mouse No. 1	No. 2	No. 3	Mouse No. 1	No. 2	No. 3
St. Catharines No. 1	4	S10++	S10++	S10++	S10−	S10−	S10−
Saskatchewan No. 1	2	D_5++++	D_5++++	D_5++++	D_4++++	D_3++++	S10++
Newmarket No. 1	2	D_5++++	D_4++++	D_5++++	S10++	S10++++	S10++
Chorley Park No. 1	3	S10−	S10++	S10−	S10−	S10−	S10−
Saint John No. 1	2	S10−	S10−	S10−	S10−	S10−	S10−
Sault Ste. Marie No. 1	3	S10−	S10+	S10+	D_5−	S10−	S10−
Edmonton No. 1	2	D_5++++	D_4++++	D_5++++	S10−	S10−	S10−
Cobourg No. 1	3	D_4++++	S10−	S10−	S10−	S10−	
Can. Arctic No. 1	2	D_5++++	D_5++++	D_5++++	D_3++	S10+	S10++
" " No. 2	2	D_5++++	D_5++++	D_5++++	S10+	S10+	S10−
" " No. 3	2	D_4++++	D_4++++	D_4++++	D_3++++	S10++++	S10−
" " No. 4	2	D_3++++	D_4++++	D_4++++	D_5++++	S10+++	S10++++
" " No. 5	2	D_5++++	D_5++++	D_5++++	S10+	S10+	S10+
" " No. 6	2	D_4++++	D_5++++	D_4++++	S10+	S10+	S10−
" " No. 7	2	D_4++++	D_4++++	D_5++++	S10+++	S10+	S10−
" " No. 8	2	D_5++++	D_5++++	D_5++++	S10++	S10−	S10−
" " No. 9	2	D_5++++	D_5++++	D_5++++	S10++	S10++	S10+++
" " No. 10	2	D_4++++	D_4++++	D_5++++	S10++	S10−	S10−
" " No. 11	2	D_4++++	D_4++++	D_5++++	D_5++	D_5++++	D_5++++
" " No. 12	2	D_4++++	D_4++++	D_4++++	D_3++++	S10+++	S10++++

D = death, S = sacrificed, Figure = No. of days after inoculation,
Signs − to ++++ indicate degree of lung consolidation.

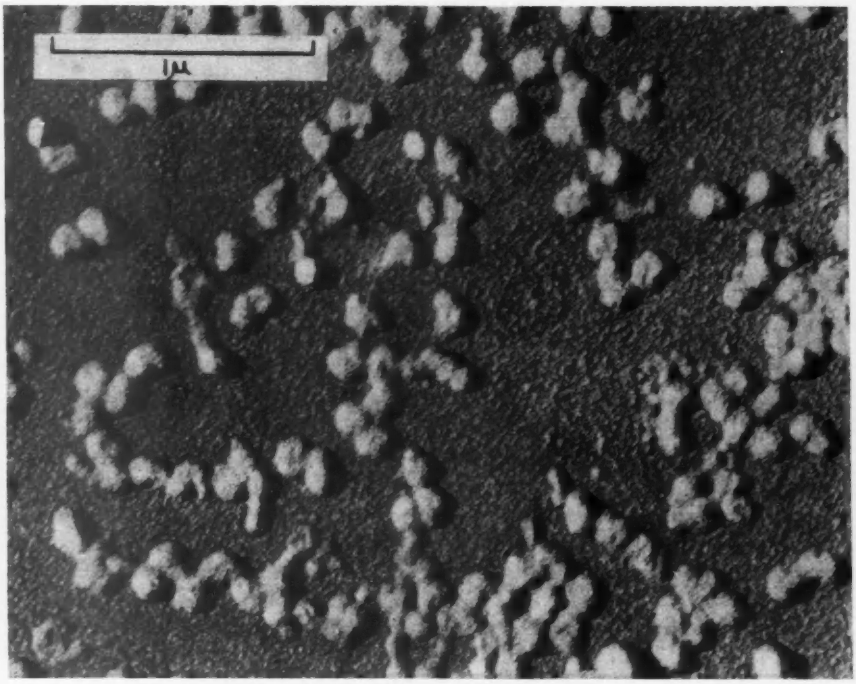

FIGURE 1.
Sault Ste. Marie Strain of Influenza Virus A—prime. (*Courtesy Dr. G. D. Scott.*)

Fig. 1 shows the Sault Ste. Marie, Ontario, strain of virus and Fig. 2 the Canadian Arctic strain no. 1 A. In size it would appear that the former is appreciably larger than the latter when examined under identical conditions.

DISCUSSION

The severity of the Cambridge Bay epidemic is of interest because of the low antibody level detected some months earlier in another isolated Eskimo community, all of which data point to lack of exposure to infection. Nagler *et al* (1949) reported that the sick Eskimos improved rapidly after hospitalization and the administration of sulpha drugs and penicillin. Secondary invading micro-organisms thus appear to have been a major contributory factor towards high mortality.

The fact that 12 typical A strains of virus were recovered from the Arctic and a serologically different type of virus designated A-prime was prevalent throughout the populated cities of the Dominion is of significance.

In an extensive study of influenza epidemics in the United States, Salk (1947) has pointed out that "influenza virus plays a much greater role as a cause of respiratory disease than had heretofore been considered." Salk (1947)

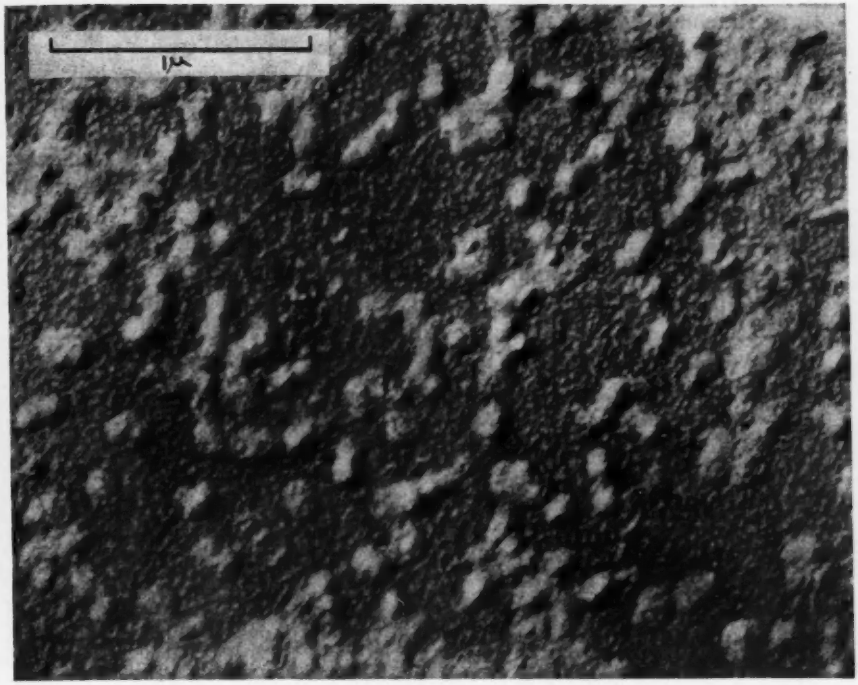

FIGURE 2.
Canadian Arctic Strain of Influenza Virus A. (*Courtesy Dr. G. D. Scott.*)

continued that "the extent and severity of influenza virus infection clearly indicate the need for an immunizing agent—and all that should be expected of influenza virus vaccine is that it will enhance the state of resistance whereby the disease produced by the specific agents may be reduced in severity or be prevented entirely." In a subsequent paper Salk (1949) emphasized that to reduce the number of cases of respiratory disease, any vaccine employed should possess specific as well as the broader antigenic coverage.

So far as Canadian cities are concerned, it is not practical to formulate proposals for immunization. The present work does, however, indicate the desirability of elevating the antibody level of Eskimos as well as white persons entering the Arctic Circle.

SUMMARY

1. During the late winter of 1949 a total of 32 strains of influenza virus was isolated from a number of cities throughout the Dominion extending from Edmonton, Alberta, to Saint John, New Brunswick.
2. The disease was mild in character and no deaths were reported.
3. All strains of virus (excepting two from Saskatchewan) were of indeterminate time but tentatively designated A-prime.

4. At the end of April a severe outbreak occurred at Cambridge Bay, Victoria Island, N.W.T. From this epidemic 12 strains of typical type A virus were isolated, including one from the lung of a fatal case. Simultaneously two further typical strains of type A virus were recovered from an outbreak in Saskatchewan. All of these were pathogenic to mice.
5. Tests on sera gathered from 224 Eskimos inhabiting two lonely settlements far inside the Arctic Circle have demonstrated the prevalent low level of antibodies to influenza viruses A and B.
6. Attention has been drawn to the need for immunizing Eskimos against infection introduced from without, together with similar inoculation of white persons entering these Arctic territories.

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An Influenza Virus Epidemic at Victoria Island, N.W.T., Canada

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EARLY in the third week of April 1949, the Department of National Health and Welfare received information that an unusually virulent outbreak of influenza, reminiscent of the 1918 pandemic, was present among the Eskimo population of the southern regions of Victoria Island, N.W.T. The department immediately undertook an investigation and on April 21, 1949, arrangements were completed. Two of the authors (F.P.N. and J.H.S.) reached Cambridge Bay, Victoria Island, by plane on April 25, where an emergency hospital had been established since April 20. On arrival at Cambridge Bay they found about fifty Eskimos hospitalized under the care of Dr. J. P. Harvey of the Indian Health Services assisted by two nurses and the dispenser of the Charles Camsell Indian Hospital, Edmonton. The latter were aided in their work by members of the Royal Canadian Air Force and the Royal Canadian Mounted Police. The data on the epidemiology were mainly obtained from a member of the R.C.M.P. who was in charge of transporting sick Eskimos to Cambridge Bay hospital and who was well acquainted with the territory and population. Part of the information on the epidemiology and most of the clinical histories were obtained directly from the patients, with the help of native interpreters.

EPIDEMIOLOGY

On March 16, 1949, four sick Eskimos from Cresswell Bay (Somerset Island, Northwest Territories) were brought by dog team to Fort Ross (see map). These subjects had not been in direct contact with white men from outside for several weeks. On arrival at Fort Ross, they were examined medically by Dr. Harvey and were found to have symptoms of a respiratory infection. The patients were transported by plane to Cambridge Bay, to be transferred to the Charles Camsell Hospital, Edmonton. While the plane was refueling at Cambridge Bay on March 16, these patients visited a nearby temporary village of igloos, inhabited by 33 Eskimos, most of whom had recently arrived at Cambridge Bay from Finlayson Island, Starvation Cove and Anderson Bay for a routine chest X-ray survey. Between the 23rd and 25th of March, approximately five days after contact with the patients from Cresswell Bay, all these subjects

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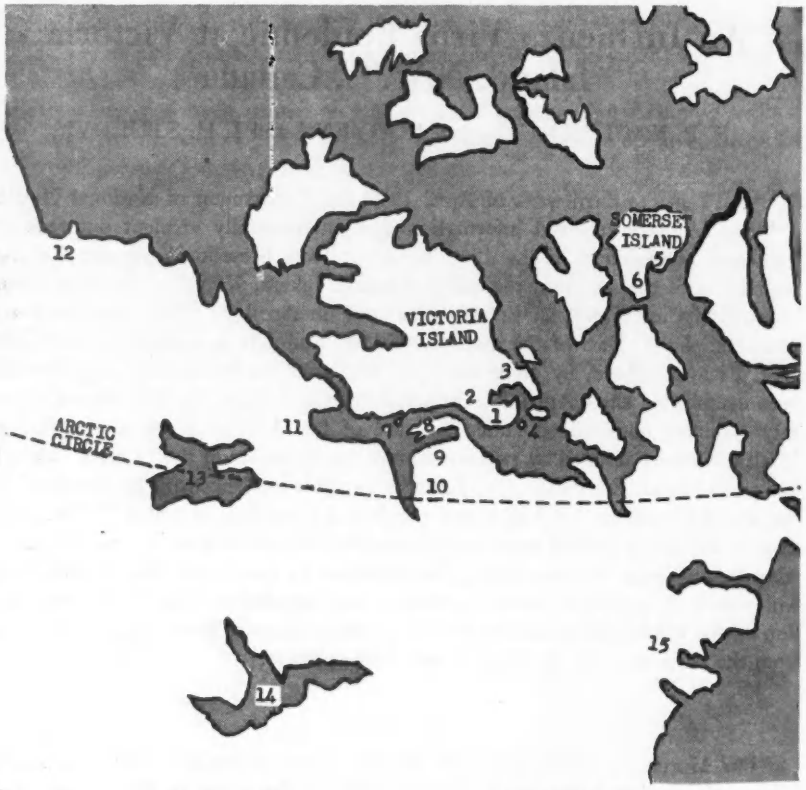
complained of headache, sore throat, and cough. In their early illness they were treated symptomatically as well as possible by white people in the vicinity (members of the R.C.M.P. and R.C.A.F. and employees of the Hudson's Bay Company).



1. Anderson Bay
2. Cambridge Bay
3. Albert Edward Bay
4. Admiralty Island
5. Cresswell Bay
6. Fort Ross
7. Finlayson Island
8. Kent Peninsula
9. Hope Bay
10. Bathurst Inlet
11. Coppermine
12. Aklavik
13. Great Bear Lake
14. Great Slave Lake
15. Chesterfield Inlet

As some Eskimos felt well enough to return to their respective settlements, two families (6 subjects) moved from Cambridge Bay to Anderson Bay on April 4, while some of the members were still sick. Later 2 adults and 2 children died at Anderson Bay.

A group of 6 Eskimos from Dease Point briefly met the Anderson Bay families on April 4. About four days later all members of the Dease Point families

became ill and 2 died at Anderson Bay within six days. The others were flown to Cambridge Bay Hospital on April 20.

Six Eskimos from the Kent Peninsula area briefly met on April 10 the Anderson Bay families at the latters' settlement. All the Kent Peninsula Eskimos became sick four days later. Three of them died at Anderson Bay and one (L.O.) at Cambridge Bay Hospital shortly after admittance.

Two Eskimos of Finlayson Island went back from Cambridge Bay to their settlement at the end of March and came in contact with other members of their and related families (12 families involving 30 people of all age groups). Four days later these Eskimos showed symptoms of the infection and 6 subjects died within ten days on this island.

Between the 8th and the 15th of April, 17 Eskimos arrived in apparently good health at Cambridge Bay from Driftwood Point, Cape Adelaide and Albert Edward Bay. These individuals had no history of previous contacts with infected Eskimos or with white people. Four and five days after their arrival they all complained of severe headaches and sore throats. One woman (M.M.) who had been admitted to the hospital on April 21 with pneumonia, died on April 24.

In summarizing the incidence of this epidemic, the Eskimo population of the southern regions of Victoria Island, of Finlayson Island, Taylor Island, Admiralty Island and the northern parts of the Kent Peninsula consisted at the time of the epidemic of about 90 people, all of whom became infected (attack rate: 100 per cent). Eighty-four natives became severely sick and 6 showed only mild symptoms of the disease. Fifty-three were hospitalized at Cambridge Bay between the 20th and 30th of April and 15 cases were treated in nearby igloos. Eighteen Eskimos died in this epidemic (mortality rate: 20 per cent); sixteen of them, before treatment could be given. All age groups were affected by this epidemic and deaths appeared to be fairly evenly distributed among individuals between 6 months and 70 years of age.

The white population of Cambridge Bay consisted of about 50 men between the ages of 21 and 35 years. These men were frequently exchanged and usually did not stay longer than six months in the Arctic. They were remarkably little affected by the epidemic. Although most of them had been in close contact with the native population, only 3 became sick with headaches and sore throats. One (A.W.) who had been at Cambridge Bay for about three years (with several short interruptions) developed symptoms of a bronchial pneumonia. He had been constantly in close contact with the sick natives for more than three weeks before he became ill.

Previous Epidemics at Victoria Island and Vicinity

There was an epidemic of a similar nature at Aklavik in 1946. A few Eskimos and some members of their families who had been sick at this time had come in contact with the present outbreak at Cambridge Bay and escaped with mild symptoms of the disease. White people and Eskimos, living at Cambridge Bay for about three years, could recall no other similar epidemics in this region.

The Clinical Course of the Disease

On questioning a number of adult patients about their past clinical histories it was observed that most of them from time to time had experienced slight colds with coughs and fever. In the present investigation most of the patients presented very similar histories. Between four and five days after contact with an infected case the first symptoms manifested themselves in the form of headaches, mainly centered behind the eyes, sore throats and elevated body temperatures in the evenings. General malaise and loss of appetite followed. On the third day of the disease, the patients complained of severe chills with pains in the throat and chest on coughing.

On admission to Cambridge Bay Hospital most patients were found to be in good physical condition.* The examination of acute and subacute cases revealed an exudative tracheobronchitis and in some of the more advanced cases a commencing bronchial pneumonia. In many of the cases there was copious discharge of yellowish and sometimes haemorrhagic sputum. In about 20 per cent of the patients the spleen was found to be enlarged and in a few instances the liver was also palpable. The other organs appeared normal and neither abnormal reflexes nor paralysis was observed in any of the cases. Body temperatures ranged between 102° and 104° in milder cases (evening readings) while temperatures of 105° were not unusual in the more severe ones.

As a rule, treatment with penicillin (crystalline penicillin in oil) was commenced immediately after the arrival of the patients, with an intramuscular injection of three hundred thousand units, followed by three daily injections of one hundred and fifty thousand units each, and then by a similar dose every second day for approximately a week. The clinical response to this treatment appeared to be very prompt and the physical improvement of the patients within the following forty-eight hours was quite pronounced. At first glance, it appeared that the body temperatures of the patients remained normal from the second day of treatment onward. However, until April 27 the patients' temperatures were taken only once daily in the mornings and, therefore, may have been misleading. This became apparent when an acutely ill patient was brought to the hospital on April 29. Although he exhibited the same symptoms and received similar treatment as the other patients, he responded less promptly. His body temperature in the evenings went up to 102° for at least three days while his morning temperatures remained normal. A similar experience was found with a second patient who was admitted to the hospital on the following day.

A few patients, under penicillin treatment, experienced a relapse in the course of their illness with fever and chills and renewed symptoms of a severe tracheobronchitis. In these cases treatment with sulphadiazine was introduced and resulted in a marked clinical improvement. The adult patients were given 1 gram of sulphadiazine every four hours for three days, followed by a similar dose every eight hours for another three days. Bicarbonates and a large amount of fluid were given simultaneously to these patients.

**During the past winter, many of the Eastern Canadian Eskimos suffered from food shortages, and nutritional problems were serious. However, the Eskimos of Victoria Island, N.W.T., depend a great deal upon the sea for their food and they did not appear to be so seriously affected.*

Laboratory Tests on Specimens from Acute and Subacute Cases

Nasal-pharyngeal washings and nasal and throat swabs were obtained from acute and subacute cases, while blood and serum samples were taken from the same and similar cases. Three Eskimos who had died in the acute stages of the disease were autopsied and specimens obtained for histopathological and other laboratory examinations.

As facilities and time were limited, on only 12 cases were blood counts and haemoglobin estimations carried out. It was found that there was quite a variation in the red cell count of these cases (3,400,000 to 4,500,000) and no relationship between the number of red cells and the severity of the disease could be established. The white cell count in these cases ranged between 7,300 and 14,000. The differential white cell count in acute cases showed a possible increase in the percentage of segmented neutrophils (66 to 82 per cent). In subacute cases, the differential white cell count appeared to be normal. The haemoglobin of several cases showed a wide variation (49 to 82 per cent Sahli). Urinalyses resulted in normal findings in about 20 cases tested.

Virology: The virological investigation of these specimens was carried out in the Virus Section of the Laboratory of Hygiene, Ottawa, and the Connaught Medical Research Laboratories, Toronto, where duplicate samples were forwarded.

Attempts were made at the Laboratory of Hygiene, Ottawa, to isolate virus from 12 throat washings by serial passage in hens' eggs. The specimens were brought to 1 in 10 dilutions in beef heart broth containing penicillin and streptomycin (200 units of each per egg). Six 12-day-old eggs were used per specimen. They were inoculated by the amniotic route and then incubated at 35°C. for 5 days. Amniotic and allantoic fluids were recovered and haemagglutination tests were carried out with fowl and guinea-pig erythrocytes by Salk's Method.[1]

On the first passage 9 out of 12 washings contained a haemagglutinating virus, while on the second passage all were found to be positive. By the third transfer the virus had become adapted to the egg and in these instances was further passaged by the allantoic route. Haemagglutinating titres as high as 1/1280 and 1/2560 for two patients (M.D. and B.T. respectively) were obtained with the allantoic fluid.

The patients' sera collected at the same time as the throat washings, and in a few instances, second samples collected about two weeks later, were tested for influenza antibodies with Lederle's viral diagnostic antigens. The sera were titrated according to Salk's method using 4 units of viral antigen per tube. The results of these titrations have been summarized in Table I. It should be noted here that the great majority of the patients had usually been sick for more than three days when admitted and had been at the hospital for six to seven days before the first samples of blood were collected. The patients, therefore, had reached the subacute or convalescent phase of their illness by then.

It can be seen from Table I that most of the sera contained a high level of antibodies against one or both of the Type A strains of influenza virus "PR8" and "FM1", and a very low titre or no antibodies against type B strain "Lee".

[1]Salk, J. E., J. Immunol., 1944, *49*: 87.

Unfortunately only a few further samples of serum were received from Cambridge Bay since April. No further samples were obtained from patients whose serum had been obtained during the very early stage of their illness. In only one pair of sera collected from one patient (J. E.) at the subacute and convalescent phase of illness was a significant rise of antibodies against the FM1 strain recorded. Local conditions precluded sampling of sera from the white population except from those under clinical treatment.

Attempts were made to isolate the virus from the organs of three autopsied

TABLE I

SUMMARY OF SEROLOGICAL RESULTS OBTAINED AT THE LABORATORY OF HYGIENE, OTTAWA

Patient		Date–1949		Inhibition titres of sera with influenza virus			
				Type A			Type B
Initials	Age	Admitted to Hospital	Blood Taken	PR_8	FM_1	Weiss	Lee
A. A.	26	21/4	27/4	256	256	256	64
B. A.	21	22/4	27/4	>4096	2048	1024	128
G. C.	15	20/4	27/4	1024	256	512	64
S. C.	45	20/4	27/4	512	2048	512	64
			12/5	512	2048	512	64
M. D.	9	20/4	27/4	128	1024	256	32
			12/5	256	1024	512	32
J. E.	53	21/4	27/4	512	256	128	64
			12/5	512	1024	256	64
P. H.	51	21/4	27/4	512	2048	256	128
			12/5	512	2048	512	128
B. K.	11	20/4	27/4	256	>4096	512	32
			12/5	128	>4096	512	32
L. K	23	21/4	27/4	256	2048	256	128
M. K.	15	21/4	27/4	1024	2048	64	128
P. K.	31	21/4	27/4	128	2048	256	<32
M. M.	14	21/4	27/4	512	2048	512	<32
D. P.	28	29/4	29/4	256	1024	128	32
B. T.	13	23/4	27/4	256	1024	256	<32
A. W.	26	29/4	30/4	1024	256	512	128

cases. The organs were ground with quartz, suspended in beef heart broth and passed through eggs in a fashion similar to the throat washings. Influenza virus, type A, was found in the second amniotic passage of the lung, liver, spleen and heartblood of one subject (B.P.) and the lung and bronchus of another one (M.M.). Studies on these strains and further attempts of virus isolation from organs of one similar autopsy are still in progress.

Investigation of identical samples of nasal pharyngeal washings, sera and autopsy specimens was carried out simultaneously in the Connaught Medical Research Laboratories, Toronto, and resulted in the isolation of type A influenza virus from all specimens of sputum and from the lung tissue of the post-mortem case M.M. (see Table II).

Bacteriology: The bacteriological investigation of the specimens was carried out at the Laboratory of Hygiene and at the Connaught Medical Research Laboratories, Toronto, but no significant pathogenic organisms were recovered. Attempts were also made at the Laboratory of Hygiene to isolate pathogenic bacteria from nasal and throat swabs and bloods of the Eskimos mentioned above. As most of these patients were under penicillin treatment when the specimens were collected, penicillinase was added to all bacteriological media used in this

investigation. However, no organisms suggestive of causal relationship to the disease were isolated; only the usual upper respiratory organisms were recovered, such as non-haemolytic streptococci, staphylococci and diphtheroids. A gram-positive haemolytic coccus of Lancefield's Group L was isolated from the bronchus of one autopsied case (B.P.). The other organs and the heart blood of this man were found to be bacteriologically sterile.

Pathology: Three Eskimos who had died in the acute stage of their illness were autopsied by one of the authors (J.S.). The gross findings of one case

TABLE II

SUMMARY OF VIRUS ISOLATION AND SEROLOGICAL RESULTS OBTAINED AT THE CONNAUGHT MEDICAL RESEARCH LABORATORIES, TORONTO

Initial of Patient	Material Examined	Virus type Isolated	Patients' serological response
A. A.	Nasal-pharyngeal washings	A	
B. A.	Nasal-pharyngeal washings	A	
L. A. B.	Nasal-pharyngeal washings	A	
G. C.	Nasal-pharyngeal washings	A	
	Serum		A antibodies
M. C.	Nasal-pharyngeal washings	A	
S. C.	Serum (two samples)		A antibodies
M. D.	Serum (two samples)		No antibody rise
J. E.	Nasal-pharyngeal washings	A	
	Serum (two samples)		A antibodies
A. H.	Nasal-pharyngeal washings	A	
P. H.	Nasal-pharyngeal washings	A	
	Serum (two samples)		No antibody rise
M. K.	Nasal-pharyngeal washings	A	
P. K.	Serum		A antibodies
M. M.	Lung tissue (post-mortem specimen)	A	
B. T.	Nasal-pharyngeal washings	A	
	Serum		A antibodies
A. W.	Nasal-pharyngeal washings	A	
	Serum		A antibodies

(M.M.) can be summarized as follows: The immediate cause of death was obviously a toxaemia. The source of infection was in the respiratory system and would appear to have begun with an acute exudative and haemorrhagic tracheobronchitis followed by a fulminating type of pneumonitis. The pneumonia appeared to be both lobar and lobular. Early abscess formation was quite definite. Many of the gross findings were obscured by the fact that the body was partially frozen. In particular the pneumonic consolidation and the fatty degeneration of the liver were not evident on macroscopic examination.

The microscopic examination of the organs revealed the following pathological features: Sections of the trachea show fairly good preservation of the mucosa in some areas; in others the mucosa seems to be eroded. The submucosa is densely infiltrated by inflammatory cells of all types, mostly lymphocytes and plasma cells, but occasional polymorphonuclears are present. There is a very marked increased vascularity in the submucosa. The inflammatory cell infiltration extends in some areas to the paratracheal mucous glands. The exudate within the lumen appears to consist of inflammatory cells lying in a fibrinous type of matrix.

Sections of the lungs confirm the gross findings of tuberculosis. This is of a fibro-caseous type. In other areas throughout the lungs extensive pneumonic

consolidation is apparent. This is both lobar and lobular in type. The swollen and distended alveoli are filled with inflammatory cells of all types, chiefly of the polymorphonuclear variety, but lymphocytes and plasma cells again abound. There are occasional pigment-filled histocytes. The lungs are intensely congested and some areas of emphysema are noted. Many of the distended alveoli contain high protein content fluid, indicating pulmonary oedema. Some of the more inflamed areas have become quite confluent, and frank abscess formation is noted. In these areas the alveolar septae have disappeared. In the small bronchi large amounts of pus have collected. The bronchial lymph nodes are hyperplastic and extremely vascular. There is no evidence of tuberculosis in the glands, but at least one gland shows early and non-specific abscess formation.

The sections of the liver show a marked central venous congestion with dilatation of the central sinusoids and compression of the central liver cells. There is very wide-spread fatty metamorphosis. This appears to be predominantly intracellular and almost every cell seems to be involved. There is considerable deposition of bile pigment and the individual liver cells show extensive hydropic degeneration.

Sections of the heart show a rather marked interstitial oedema. There is a moderate and fairly early interstitial fibrosis also present. The individual muscle fibres show a marked perinuclear deposition and lipochrome pigment suggesting a brown atrophy. There is some fragmentation of muscle fibres and these show a considerable variation in tinctorial properties, being pale, with indistinct cross striations in some areas and more deeply stained in others. The oedema is especially marked around the small blood vessels.

In sections of the kidneys the proximal and distal convoluted tubules show a very advanced albuminous type of degeneration. They are quite swollen and granular. There is no evidence of any interstitial inflammatory reaction. Adrenals appear of relatively normal histological structure.

The anatomical diagnosis of the autopsy of the second case (B.P.) presents many features identical with the previous one (M.M.) and the chief pathological change was obviously an overwhelming infection of the respiratory tract, including trachea, bronchus, bronchioles and the pulmonary parenchyma. This took the form of an exudative and haemorrhagic inflammatory reaction which presented unusual histological changes. The lumina contained masses of polymorphonuclears, fibrin and blood.

In the lungs the chief processes appeared to be a pulmonary oedema with acute diffuse pneumonitis. It is probable that the abscess formations which were so prominent in this case were due to secondary invaders. The ante-mortem blood clot in the right auricle is difficult to explain but may have resulted from a terminal arrhythmia consequent upon a toxic myocarditis.

The anatomical diagnosis of the third case (L.O.) at autopsy is very similar to the previous ones and can be described briefly as follows. The cause of death appears to have been toxaemia with organ degeneration, attendant upon an acute infection of the respiratory tract. At the time of death, there existed an acute exudative tracheobronchitis, an acute bilateral lobar and bronchopneumonia, with early abscess formation, toxaemia with organ degeneration and a healed unilateral pulmonary tuberculosis.

Discussion

The epidemic at Victoria Island apparently originated in an area which had not been visited by white men from outside for more than one month. It is possible that the causative agent of this epidemic had been introduced into Cresswell Bay from without by other Eskimos, who had derived immunity through recent contact with white persons. The white population of Victoria Island remained remarkably free of serious infections at the same time and one can therefore assume that they were immune to the infective agent. Had circumstances allowed it, we would have carried out a survey of the relative antibody levels of Eskimos and white persons to A and B strains of influenza virus, but such was obviously impossible during the Arctic winter. The first sera of nearly all Eskimos were collected at least eight days after onset of their disease and could, therefore, not be accepted as acute phase sera. Only in a few instances was it possible to secure paired sera which showed a rise in antibodies against influenza virus type A. However, the clinical course of the disease and the isolation of influenza virus from the throat washings of Eskimo patients, and organs and blood of post-mortem cases, with the absence of other pathogenic organisms in the specimens, leave little doubt that the causative agent of the epidemic was influenza virus A. The good clinical response to penicillin and sulphadiazine was probably due to the control of secondary bacterial invasion.

While this report was being prepared for publication, the authors were informed that the epidemic had spread westwards and had affected the Eskimo population around Coppermine. The clinical picture of the disease and the case fatality rate here were similar to those described above for the Cambridge Bay outbreak.

Summary

An epidemic of virus influenza in the Eskimo population of the southern regions of Victoria Island, N.W.T., and vicinity caused an attack rate of 100 per cent (90/90) and a case fatality rate of 20 per cent (18/90). The great majority of deaths occurred in Eskimos who had received no medical treatment (16/18). Penicillin and sulphadiazine appeared to have been of great value in preventing secondary bacterial infections and further deaths. The white population (approximately 50 men) of Victoria Island were relatively unaffected by the epidemic and medical treatment was required in a single case.

Influenza virus type A has been isolated from all throat washings of the Eskimo patients. Convalescent sera of these patients contained a high titre of antibodies against the influenza virus strains FM1 and PR8. Influenza virus type A was isolated from the lung, liver, spleen and heart-blood of one, and the lung and bronchus of a second fatal case.

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Nomenclature and Interpretation of Results of Serological Tests for Syphilis

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CLINICAL and epidemiological evidence indicates that the incidence of syphilis in Canada, at the present time, is declining. This decline is occurring in spite of the fact that there has not been any discovery or introduction of an immunizing agent nor do we have, as yet, any specific diagnostic serological test. Considerable progress has occurred, however, in the fields of epidemiology, diagnosis and treatment, all of which has been conducive to the location of early cases and the control of communicability.

Other than the darkfield microscopic examination there is not a laboratory procedure which serves as a specific diagnostic test. Therefore reports of serological tests for syphilis must be interpreted in the light of available anamnestic and clinical data. During the past few years considerable data have been accumulated regarding serological test results in persons suffering from non-syphilitic disease or infection. False biological or pseudo-syphilitic positives now form a significant proportion of the total positive reactions found on routine examination. It is logical to expect that this proportion will increase as the incidence of syphilis declines. It is of growing importance, therefore, that serological test results be related to clinical and epidemiological findings, and that a diagnosis be reached only after the elimination of any possible false biological or pseudo-syphilitic causes which may exist.

This does not mean, however, that we need have any less confidence in the standard serological tests. To lose confidence in the value of these tests because we have come to a greater realization that they are not as specific as we formerly thought, is merely evidence of lack of appreciation of their true significance. If we have endowed them with unwarranted qualities of specificity, it has been our error alone. These tests as carried out today in a modern laboratory are giving a more accurate interpretation of serum reagin content than has ever been provided heretofore. The tests were never intended to do more than provide this information. The fact that serum reagin concentration rises significantly, in many circumstances other than that of a syphilis infection, simply means that the physician must use greater skill and knowledge in arriving at a diagnosis and that he cannot escape this responsibility by transferring it to the laboratory.

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One laboratory examination is never sufficient as supporting evidence for a diagnosis of syphilis, even in the presence of clinical manifestations. The only exception is in primary syphilis where organisms morphologically typical of *Treponema pallida* have been found by a bacteriologist who is experienced in this examination. In the absence of clinical signs, blood specimens should be examined on three occasions, at intervals of three weeks. It is imperative that laboratories perform quantitative tests on all specimens reacting to qualitative tests. Frequently the qualitative tests will remain positive throughout these three examinations, but the quantitative test will demonstrate a decrease of reagin during this period. A reduction in titre of the quantitative test, without the administration of treatment, is the earliest indication that the laboratory can provide of a possible false positive reaction. It is important that the series of specimens for quantitative examination be submitted to the same laboratory. A thorough clinical history, emphasizing any concurrent infection or disease, covering the previous three months, and a thorough physical examination is also essential.

It is disastrous to place the stigma of syphilis on a non-syphilitic patient. It is not disastrous to withhold treatment from a case of syphilis until the possibility of a false positive reaction can be eliminated. These facts should be made known to undergraduates in our medical teaching centres and to graduates in medicine by means of an appropriate educational program.

At one time diagnostic tests were reported according to the intensity of the reaction. Such tests were reported in the terms of 1, 2, 3 and 4 plus reactions. Fortunately, practically all laboratories at the present time have abandoned this method of reporting the results of a qualitative test. The terms used by the majority of laboratories at present in reporting the diagnostic tests are *positive, doubtful* and *negative*. Unfortunately there has been a tendency on the part of authors of certain tests to introduce the term *weakly positive*. Every attempt should be made to discourage the introduction of any terms other than those which would signify a positive, doubtful or negative when reporting a qualitative test. If the reaction is not positive, then it is doubtful. If the reaction is not doubtful, it is positive. If there is no reaction, it is negative. The tendency to report weakly positive tests is a reversion to the old practice of reporting 1, 2, 3 and 4 plus reactions, using different terminology.

It is unfortunate, perhaps, that the terms *positive, doubtful* and *negative* were ever adopted. These words have inferred to the general practitioner that a *positive* result meant his patient had syphilis and a *negative* result meant that syphilis was absent. A constant educational program is necessary to correct these fallacies, which have been developed through the years. It would have been preferable to state a reaction was present or not present in the qualitative tests. In quantitative tests it would have been preferable to state the greatest dilution of serum showing a reaction, as is done in agglutination tests for enteric diseases. The recommendation of Harris of the Venereal Disease Research Laboratory at Staten Island, that quantitative tests for syphilis be reported in "dils.", is a step in this direction.

The use of the word *doubtful* when reporting reactions which do not meet the criteria for a positive report, has caused, and is still causing, considerable misunderstanding among general practitioners. Many interpret the doubtful

report to mean a presumptive diagnosis of syphilis or a "mild" infection. Others believe that the serologist who examined the specimen of blood is in doubt as to the reading of the test he has performed. Many physicians become not a little annoyed when specimen after specimen is reported as "doubtful—please submit further specimens". It should be impressed upon physicians that it is the duty and responsibility of the serologist to report exactly what he finds. He does not see or examine the patient and, as a matter of fact, often does not even know his name. He receives a specimen of blood and performs a highly standardized test, protected by extensive controls. He reports what he finds—even though it may not be what was expected or desired. The report that is issued is of value only in the light of clinical and other facts respecting the patient from whom the specimen was taken.

The so-called doubtful reaction is a definite reaction based upon a definite criteria of observations. The writers suggest that its most significant characteristic justifies a change in nomenclature. Basically the report is doubtful because it is neither positive or negative and therefore it might better be said to be "inconclusive". In dictionaries we find that this word has the following meanings: "not conclusive in evidence or argument; not leading to a determination or conclusion; not decisive or convincing; indeterminate". On the other hand, we will find that the word "doubtful" is given such meanings as "full of doubt; having doubt; not settled in opinion; dubious; ambiguous; uncertain; vague". It is our belief that the word "inconclusive" therefore better conveys the findings of the serologist. To the physician it still may be annoying or on occasion even disconcerting, but it should indicate clearly to him that he must seek for any "conclusive evidence or argument" elsewhere than in the serum of his patient.

The close integration of all services and the close cooperation of all persons concerned in syphilis control procedures is of growing importance as the incidence of this disease declines. The demands on the general practitioner are many and therefore it is our duty to assist these members of the profession who are so essential to the effective implementation of any control program. We must keep them informed regarding the principles, application and limitations of serological tests, but above all we should use terminology that is simple and informative when reporting the results of laboratory examinations.

In view of the above considerations, the Department of Health for Ontario is planning to institute the following changes in nomenclature:

1. Blood specimens failing to show a reaction and previously reported as *negative* will be reported as *no reaction.*

2. Blood specimens showing a reaction and reported previously as *positive* will be reported as *reaction present.*

3. Blood specimens showing weak reaction of such intensity that they would not have been regarded previously as positive and would have been termed *doubtful* will be reported as *inconclusive.*

4. Quantitative tests will be reported as the greatest dilution showing a reaction.

5. The word *negative* will be placed in brackets after *no reaction, positive* after *reaction present,* and *doubtful* after *inconclusive* until such time as physicians become accustomed to the new terminology.

Teamwork in Health Education

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FOR the sake of teamwork, coordination can be defined as "cooperation properly directed", or, even better, "cooperation automatically established". For the purpose of health education we must assume, although we may be taking a lot for granted, that all health educators have been trained in public health, and that their teachings are pedagogically sound and scientifically accurate.

As I have been asked to speak "about getting the members of the health department to work together as a team", I feel that we should consider the relations between all health educators, including those outside the health department, firstly on the vertical plane as between federal, provincial and local agencies; secondly on the horizontal level, as between the various individuals engaged in health education and expected to operate as a unit.

Health educators working at different levels, in official or voluntary agencies, should be in full agreement on their necessary cooperation for rendering an adequate public service, as a matter of policy and according to their general philosophy of education. Meetings like this one and the annual health education conferences called by the Department of National Health and Welfare afford excellent opportunities for the discussion of policies, as well as objectives, methods and materials.

From the policy agreed upon will derive properly defined functions that will guide all health educators in the implementation of their respective program. In the British North America Act of 1867, no mention was made of health education in Canada and its provinces, the mere idea of it had not been conceived; therefore here is a field of joint responsibility where coordination is to be realized on a voluntary basis. In other fields of the same category, the Federal Government only helps provincial departments, usually on request, to provide the health services for which they are responsible, by means of grants, by making surveys, or by serving as a source or an exchange of technical information.

Such a Federal undertaking, well received by the Provinces, has been the preparation of health education materials; in recent years their production has been greatly intensified. I wish to repeat what I said last year in Vancouver: "Their preparation requires resources that only national organizations possess.

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If something in health education should be centralized, this is it. . . . The material that should be prepared locally is that offering a local solution to a local problem. Any piece of material dealing with general health, the same everywhere, should be prepared centrally. To do otherwise results in duplication, waste, and usually inferior quality." The validity of the above statement has not yet been questioned, to my knowledge. It is hardly necessary to point out that a *sine qua non* condition is regular consultation between federal and provincial authorities in the planning and production stages of proposed materials.

The distribution of those materials, however, is an altogether different problem; this can be assimilated to the whole range of health services that are the statutory duties of local health departments (as delegated to them by the provinces). The authority of the medical officer, so channeled by provincial statutes, is respected by all who admit his responsibilities; is he not the one who is bound to render such recognized services as immunization and other control measures against communicable diseases, school medical examination, sanitary inspection, and, we must add, health education?

In order to maintain an established and fully justified relationship, no provincial technician would go to a community without the knowledge of the local medical officer, and there give a talk, show some pictures or prepare an exhibit on a health subject for a group meeting. Similarly, requests for health publications that are often mailed to the provincial department by individuals are promptly returned to the proper county health unit.

The responsibilities of the federal department are being adjusted along the same lines, for one can readily imagine the confusion that would arise if it distributed to the public, lists of publications that the local health authority has not in stock or perhaps does not want to use at all. It must not by-pass the provincial department and then go over the head of the local authority to give an individual a pamphlet he can obtain from his own health officer. Any such breach of relationships is sure to bring a conflict of authority and cannot be for the common good.

I would venture to think that voluntary agencies should adopt a similar line of conduct. The following example will show what can result from a different procedure. In a province, a voluntary agency is sponsoring a series of radio programs over a powerful station and in this way reaches a large section of the population. This agency distributes free literature that it obtains from federal and provincial sources and uses the procedure to evaluate its educational undertaking. So here we find a provincial ministry of health which has a sound policy of returning individual requests for literature to the local health officers concerned, but is asked by a voluntary agency for publications that will be distributed to individuals over the heads of the local health officers.

A conclusion is obvious if the recommended procedure is to be followed by federal, provincial and local agencies, both official and voluntary: it is that, in all circumstances, the public be invited to send its requests for literature to its local health department. It then becomes the responsibility of the health officer to decide which publications are suitable for distribution to the population under his jurisdiction and to avail himself of supplies accordingly. Exceptions

to this rule should be made only with his consent and each one brought to his attention.

On the horizontal level, the need for cooperation is just as evident between the various individuals engaged in health education; that is, the health educator and the other public health workers: health officer, public health nurse, sanitarian, school health teacher, voluntary agency technician, and even members of allied professions.

Agreement is now being reached that health education should not be specialized. Just as generalized public health nursing is now the accepted procedure, it is felt also that, at the *public* level, health education should not be given by specialists. These obviously are fitted for and should be assigned to professional training, but their outlook on a particular problem and its solution should be studied in regard to other needs in a total program and the terminology they use in their teachings must be carefully interpreted to the people.

This is equally true at the provincial level. At the Conference of State Directors of Health Education held in Boston on November 8, 1948, the question of the employment of health educators in specialized fields by State Departments of Health was discussed. The Conference agreed that their assignment to various divisions other than the Health Education Division is a step backward. Several directors pointed out that the demand for health educators in specialized fields decreases in the same proportion as the Health Education Division expands.

The above should not be construed as a ban on the use of resource persons by a health educator in various circumstances—on the contrary, this may be most desirable and sometimes is necessary; but it imposes special duties on the health educator. He remains responsible for assuring correct interpretation, desirable uniformity and adequate coverage, avoiding repetitions as well as omissions.

It becomes obvious that such coordination can result only from efficient teamwork, and this in turn calls for a strict discipline from people that already have the right attitude of mind. Any cooperative undertaking brings forth the problem of relations between workers of similar professional interests, and usually relations are no longer a problem as soon as people get together and discuss them.

Personal contacts in private interviews and staff meetings are the easiest way for people to find how they can work together. The formula certainly is not new, but its application could be improved and expanded by public health educators. Those who already act accordingly with their colleagues of the health department could reap worthwhile benefits if they would extend the same procedure to the voluntary agencies in their communities.

Teamwork has been an important element in the control of communicable diseases; the procedures are now pretty well established and give what they can from case reporting to terminal disinfection. Only when those engaged in health education do likewise operate as a unit, will they render a really efficient service.

Cooperation springs from an attitude which, like all attitudes, is the fruit of acquired knowledge and habits; these in turn are the results of the pro-

fessional training to which one has been subjected. It is therefore high time for the schools of public health to realize that those who are to work together should train together. Thousands of years ago, men learned that soldiers must train together for concerted action in battle; musicians, sportsmen and actors were quick to apply this elementary rule of training in their realm. But for public health work, several if not most universities still train health officers in one school and public health nurses in another; health educators, sanitarians and other students take tightly partitioned courses specially designed for each category. No school of hygiene can dodge this responsibility since the advice that Doctor Anderson gave in Quebec two years ago and which I should like to quote in his own words. I quote.

"I would therefore advance for your consideration this . . . principle, viz., that, so far as possible, isolationism in professional training practices should be replaced by a system whereby the various professional groups that are to be welded into a public health team should be trained as a group with an understanding of each other's problems, approaches and basic philosophy. I believe that this coordinated training can further be carried to the point where, to a limited degree, certain basic courses can be taught to the group as a whole without interfering with the opportunity for each type of professional worker to enrich his knowledge within his field of specialization. If this can be accomplished, I believe we shall see not only a more harmonious but also a more efficient team of public health workers".[1]

I should like to point out that Doctor Anderson's suggestion is as valid for field work practice as for academic training. One can readily see many courses to be taken in common by different categories of students, in addition to the seminars intended for all; but, as some schools have shown the way, one can well imagine those different students being sent in the field as a team on various assignments, all related to one problem calling for a cooperative solution.

Such academic and practical training in common would certainly give a better understanding of the competence and limitations of resource persons. All would gain a correct knowledge of what one can expect from others but is himself expected to do for them. No doubt a true pattern would emerge of the divided but coordinated responsibilities of the members welded together as a team by a satisfactory integration of their professional training.

Only when good internal relations have become a prerequisite of public relations, can all those engaged in health education, aiming at a high but worthy objective, strive together to attain it in perfect cooperation.

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[1]Anderson, Gaylord W.: Professional Training for Public Health. Canad. J. Pub. Health, 1948, **39**: 1.

Progress in the Treatment of Typhoid Fever with Vi Bacteriophages

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IN two previous preliminary reports (1, 2) we described the results obtained from the treatment of 20 typhoid fever cases with Vi antityphoid bacteriophages I, II, III, IV of Craigie and Yen (3). These two reports indicated the modification which we effected in the original method of Knouf, Ward *et al.* (4), who treated 56 typhoid cases employing only specific Type II bacteriophage. We used a mixture of I, II, III and IV phages. The polyvalent phage was diluted with 500 ml. of 5 per cent glucose solution and administered by intravenous injection, with the drip method, in accordance with the technique prescribed by the above-mentioned authors. The polyvalent phage possesses the advantage of serving for the treatment of all typhoid cases, even of those in which the inciting strain of *Salmonella typhosa* is resistant to phage II. The favourable results obtained from these first 20 cases (no deaths) encouraged us to continue these experiments.

We have, however, further modified the polyphage and altered the method of administration. To the four Vi phages of Craigie and Yen, we added two new Vi phages which we isolated in the Province of Quebec and which we have designated as Type V and VI phages. These two phages, producing very small plaques, possess, however, a remarkable power of diffusion (attack), resulting in plaques of 5 mm. *in vitro* with homologous cultures. They are not neutralized by antisera I, II, III and IV and their antisera do not neutralize phages I, II, III and IV.

The drip method of injection requires a rather complicated equipment and is not readily adapted to treatment in the home. Upon modifying somewhat the concentration of the polyphage and on eliminating all bacteria not lysed in the course of the preparation of the phages, direct injection in the vein was tried, employing 3 or 4 injections at intervals of two days. By this direct method, 36 typhoid cases were treated in the Province of Quebec in 1948. Some twenty cases have also been treated with this polyphage outside the Province, but we have had no bacteriologic control of these outside cases.

From reports received from the physicians interested, it appears that, clinically, the results obtained with this direct treatment are similar to those secured with the drip method, as reported by Knouf, Ward and their collabo-

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rators and also by ourselves. A few hours after the injection the patient's temperature rises 3° to 4°F. and remains at this level for 3 to 5 hours. The majority of the patients experience, a few hours following the injection, a chill lasting 20 to 30 minutes. The temperature then falls rapidly to 94° to 97°F. After the subsequent injection the temperature rise and fall are less marked. Following the 3 or 4 injections the temperature is stabilized between 97° and 98°F. When the treatment is given early in the disease, during the septicemic stage, blood culture rapidly becomes negative and no positive faeces are obtained. Treated at this stage, some patients are completely cured within ten days. If treatment is begun when the faeces are already positive, the bacteriologic results vary considerably: the stools of some patients will be negative a week or two after treatment, whereas those of other patients may remain positive for several weeks and some patients may become germ carriers. Nevertheless, the efficacy of the treatment, as regards disappearance of symptoms and temperature, is similar in all cases.

Of the 36 patients treated in 1948, 21 were completely freed from typhoid organisms as determined by finding two samples of faeces, collected at an interval of two weeks, to be negative. Two patients remained carriers; one of these was later treated with aureomycin with no effect. The status of the other thirteen persons is not definitive because the required release specimens have not yet been submitted for examination. One patient died following meningeal complications. The mortality rate for the group is therefore 2.7 per cent, whereas that for the 56 patients treated in both 1947 and 1948 is 1.8 per cent. Knouf, Ward *et al.* reported a mortality rate of 5 per cent for the same number of cases.

In January, 1949, we prepared a new lot of polyvalent phage, the concentration of which varied in different ampuls from 10^{25} to 10^{30} particles per ml. The phages were propagated on sensitive cultures in a definite medium containing no meat infusion. The distribution in ampuls, the sterility tests and the tests on animals were done at the Institute of Microbiology of the University of Montreal. The final titration of each phage in the mixture was done at the Division of Laboratories of the Quebec Ministry of Health. Up to June 1, more than 550 ampuls have been gratuitously distributed, many to various foreign hospitals and laboratories.

Early in February two small outbreaks of typhoid fever occurred in the Province, with two different types of *S. typhosa* involved, Types C and E_4. The 13 cases from these outbreaks, aged from 16 months to 17 years, were hospitalized in the same ward at Ste. Justine Hospital, Montreal. All were treated with polyphage. Thanks to the collaboration of the physicians and authorities of this hospital, a number of experiments were made, the results of which may allay, in some measure, apprehensions such as those expressed, in a personal communication from Doctor James Craigie, of London, as follows:

"Your news about the treatment of typhoid cases with polyvalent Vi phage is most interesting and I look forward to hearing of the results of later developments in preparing and administering the phage. One thing, however, worries me about clinical trials. That is the risk of occasional untoward results—collapse or death—which might discourage more

extensive trials. I have in mind the danger of increasing the load of Vi and O endotoxins temporarily beyond the amount the patient can stand. A certain additional amount will be introduced with the phage preparation. If the phage produces prompt and massive lysis *in vivo*, further amounts of Vi and O endotoxins will be liberated. I think, therefore, that a detailed study of Vi and O antibody levels in the patients' blood, before, during and after phage administration would be helpful. The antibody titres might, with experience, guide decision as to whether the phage be given rapidly or by continuous intravenous drip.

"After the commencement of phage treatment, blood samples should be taken at 6 to 8 hours' intervals for the first two days to see if the changes in Vi and O antibody level are rapid or significant. Agglutination tests, provided that reference Vi and O sera are used in each set, will serve unless the results are of such a nature as to warrant mouse protection tests.

"The blood might also be titrated for phage and tested for phage antibodies. Phage antibodies develop rapidly in rabbits. If humans are as responsive, the continuation of phage injection beyond a week is unlikely to be of value since the injected phage will be promptly neutralized."

Twelve of the thirteen patients were tested before and after polyphage treatment as suggested by Doctor Craigie, except the very young from whom it was impossible to collect the required number of blood samples. One child died from pneumonia and pancarditis, some days after admission to the hospital. The following examinations were made:

Before every polyphage treatment, blood for sero-diagnosis and culture, and faeces were collected; the blood and faeces were examined for presence of *S. typhosa;* the type of *S. typhosa* was determined; the titres of Vi, O and H antibodies in the serum of the patient were determined; the power of the patient's serum to neutralize Vi phages was tested.

After injection of the polyphage, the titres of Vi, O and H antibodies in the patients' serum were determined at regular intervals; the power of the serum to neutralize Vi phages was tested; bacteriophages were sought in the blood and in the faeces; blood, faeces and urine were examined for the presense of *S. typhosa;* tests were made to determine whether the bacteria isolated were of the V or W form.

The results of these examinations may be summarized as follows:

Two of the twelve patients showed the presence of Vi antibodies in their sera before treatment.

The dilution titres of O and H agglutinins in the sera before administration of the polyphage varied between 1:500 and 1:5000.

No patient's serum neutralized the six Vi phages before treatment.

In every case, *S. typhosa* was isolated either from the blood or from the faeces. All cultures were of the V form and typable.

For administration of the polyphage, the physicians of the hospital, who had already treated some twelve patients previously, tried successfully a new procedure. At 9:00 a.m. 1 ml. of the polyphage was injected directly into the vein; this was followed by an injection of 250 ml. of 5 per cent glucose for hydration of the patient. The rise in the patient's temperature was noted every 15 minutes. If within 3 to 4 hours after the injection the temperature had not reached 106°-107°F., another 1 ml. of the polyphage was injected. On the 3 or 4 following days the same treatment was repeated. The physicians found no

unfavourable indication following this massive treatment. The typhoid aspect disappeared and the temperature dropped within a few days after the treatment.

We noted no increase in the Vi agglutinin titre in the serum of any of the patients, even in those which, before treatment, showed the presence of such agglutinins; the titre of the O and H agglutinins, however, increased rapidly within a few days to reach levels as high as 1:25,000.

Neutralizing antibodies appeared in the first week after polyphage injection. Phages I, II and III wer neutralized first, to be followed later by phages IV, V and VI.

The patients were freed from *S. typhosa* more or less rapidly, depending upon whether the treatment was administered early or late in the course of the disease. None of the twelve patients became carriers.

Of the cultures isolated after the treatment, 99 per cent were of the V form and of the same type as before treatment.

Bacteriophages were found in the faeces a few hours after the treatment. We did not find them, however, in the blood; perhaps some question of the technique employed may be involved here.

In our previous reports we noted an early appearance of Vi antibodies in the sera of treated patients; to our surprise, we found no production of such antibodies in sera of the patients treated with the new polyphage. Naturally, we desired to know the reason for this difference.

The sera neutralizing phages I, II, III, IV, V and VI are prepared by injecting into rabbits the corresponding concentrated phages, each of which, in turn, is prepared by propagation on sensitive cultures. These cultures, being of the V form, must contain Vi antigen in order that propagation may take place, but they nearly always contain a certain proportion of bacteria of the W form—O and H. By agglutination tests of these sera with Vi, O and H antigens, we have found that, contrary to expectations, the six neutralizing sera agglutinate not at all the Vi antigen, but do agglutinate O and H antigens to titres from 1:10,000 to 1:15,000.

We repeated the experiments with rabbits, but injected phage II propagated exclusively on the strain Bahtnagar Vi I which is characterized by absence of O and H antigens (5). The phage was propagated on this V-form strain, after it was purified several times by isolation from a single plaque and by taking care that lysis was complete and that non-lysed bacteria were eliminated by centrifugation. A rabbit was injected with this Vi bacteriophage and the results observed follow:

March 8. Blood sample: Ty.O:— Ty.H:— Ty.Vi:—
Neutralization: O

March 8. 1.5 ml concentrated phage injected.

March 9. Blood sample: Ty.O:— Ty.H:— Ty.Vi—
Neutralization: O

March 10. 1.5 ml phage injected.

March 11. Blood sample: Ty.O: + 1/50, Ty.H: + 1/50, Ty.Vi:—
Neutralization: O

March 14. 1.5 ml phage injected.

March 16. Blood sample: Ty.O: + 1/937, Ty.H: + 1/1750, Ty.Vi: —
Neutralization: 50% in dilution 1/10
25% in dilution 1/20
5% in dilution 1/40

March 22. 2.0 ml phage injected.

March 25. Blood sample: Ty.O: + 1/5625; Ty.H: + 1/7500, Ty.Vi: —
Neutralization: 99.99% in dilution 1/320
99. 9% in dilution 1/640
50.% in dilution 1/1280

These results indicate that the bacteriophage Vi does not produce Vi antibody but rather O and H antibodies. Using the same strain Vi I of *S. typhosa,* and killing it with formol, we find that if this is injected into the same animal, Vi antibody is produced in a few weeks without any increase in the O and H antibodies. Thus, the entire bacteria produce Vi antibody, whereas the same bacteria, disintegrated by Vi bacteriophage, produce only O and H antibodies, even when the strain is not supposed to contain the corresponding antigens. We have verified the suspicion that our first polyphages contained unlysed, dead bacteria of the V form, and it was for this reason, apparently, that the sera of our earlier patients showed the presence of Vi antibody.

The results of these experiments suggest the manner in which the bacteriophage acts in the phage treatment of typhoid fever and also suggests the reason for its failure to free carriers from harboured bacteria. Apparently, it is the antibodies or protecting endotoxins, rapidly assimilated, which cause the disappearance of the symptoms of the disease; the bacteriophage itself, in contact with the bacteria in the body of the patient, liberates new protecting endotoxins by destruction of the bacteria. This lysis thus appears to be the indirect cause of the cure as regards symptoms. In carriers this phenomenon does not occur because they are already immunized; and the bacteriophages cannot reach all the bacteria because some of the latter are distributed in difficulty accessible locations where few or no phage particles can reach them.

These experiments explain also another puzzling phenomenon: the absence of Vi antibody in the sera of the great majority of the patients and the presence always therein of O and H antibodies. However, it is almost always in the V form that bacteria are isolated from these patients and these V forms are not agglutinable by experimental O and H sera. The bacteria destroyed, whatever be the mechanism employed, produce O and H antibodies; whereas those bacteria not destroyed, as found in convalescents who have long harboured them and in carriers, apparently produce only Vi antibody with more or less O and H antibodies.

Summary

New methods of preparation of polyphages and their administration for treatment of typhoid fever are described. The results of a detailed study of the response, as regards appearance of various antibodies, bacteriophages and bacteria in the sera or faeces, of a group of 12 patients, before and after phage treatment, are reported. A theory of the action of bacteriophages on the bacteria in treated patients and in carriers is offered.

ACKNOWLEDGMENTS

Our thanks are due to the physicians and the hospitals who have kindly tested the polyphage treatment; to Mr. M. H. McCrady, Chief of Laboratories, for his continued encouragement and his aid in the preparation of this report; to Dr. M. Saint-Martin, Bacteriologist, and to Dr. R. Cyr, Associate Bacteriologist, for their collaboration in the experimental work; to Dr. J. Craigie for his advice; and to Miss I. Martin for her valuable assistance in the technical work required in this study.

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HAVEN EMERSON, A GREAT PUBLIC HEALTH LEADER

ON the occasion of the seventy-seventh annual meeting of the American Public Health Association, held in New York last month, tribute was paid to one of the most distinguished and honoured leaders in public health, Dr. Haven Emerson, by the awarding of a special Lasker Award in recognition of his great contribution. It will be recalled that, in addition to recognizing scientific research, individual awards are made each year by the Albert and Mary Lasker Foundation for outstanding administrative accomplishments in the promotion of public health, as well as one or more group awards to large collaborating groups of workers or agencies for unusual contributions to research or to public health. The recipients of the group awards receive a hand-illuminated citation and an engraved symbolic statuette of Winged Victory, and the recipients of individual awards are given, in addition, a stipend of one thousand dollars. The donors have also made available a special award of twenty-five hundred dollars for a contribution to medical science or public health of exceptional importance. This award is not made annually but is reserved by the Association as a means of recognizing unusually valuable accomplishments. This year the Lasker Awards Committee unanimously urged that a special award be made to Dr. Haven Emerson. In presenting the award at the first general session of the meeting, Dr. George Baehr, chairman of the Committee on Lasker Awards, summed up Dr. Emerson's contribution thus:

"Dr. Emerson has for years carried the torch of public enlightenment concerning the need for complete local health services to every section of this country. His extraordinary energy and perseverance seem finally to have convinced the people and the legislators throughout the land that in the establishment everywhere of local health services lies our public health salvation. This accomplishment has also been due to his encyclopedic knowledge, his mastery of debate, his broad experience, and his unusual skill in the effective use of the English language. The public will never realize the full measure of the debt it owes to him, but this Association which he has long represented is anxious to reveal its appreciation of the man and his work by a special Lasker Award for 1949."

A second tribute to Dr. Emerson took the form of a luncheon session, sponsored by the Epidemiology Section, to mark his seventy-fifth birthday and to present more fully his work as a public health statesman, as a teacher, and as an epidemiologist. A very happy suggestion had been made by Dr. Emerson's friends that a selection of his papers, representing the wide range of his interests, be published in one volume to mark the occasion, and this was generously facilitated by the W. K. Kellogg Foundation. The volume* includes papers in the many fields of public health, population problems, problems of the American Indian, alcoholism, and many other subjects, and the luncheon provided the occasion for presenting the first copy to Dr. Emerson. Addresses were given by Dr. Charles F. Bolduan, former director of health education, New York City Department of Health; Earle B. Phelps, C.E., College of Engineering, University of Florida; and Dr. A. J. Chesley, secretary and executive officer of the Minnesota State Board of Health. Excellent as were these addresses, it is the words of Dr. Emerson, in his appreciation of the occasion, that will remain with all who heard them. Few men are as gifted as he in his ability to express his thoughts with such clarity and apt phrasing. His response to this expression of good will by his friends, among whom were many former students, was characteristically sincere and reflected his innate modesty. Dr. Emerson has been a close friend of Canadian public health and it was a delight to those from Canada to participate in this session and to join in honouring one who has given so much to the advancement of public health on this continent. It was an occasion long to be remembered.

THE PHYSICIAN AND LABORATORY SERVICES

THE practice of medicine in our day is being provided with an increasing number of diagnostic aids which are becoming so acceptable in our hands that we are in danger of being helpless without them. We have only to contemplate the prospect of the practice of medicine without the aid of modern laboratory services to realize how great a significance we place upon the reports of the findings.

To suggest that the modern laboratory is providing an increasing measure of the evidence upon which diagnoses are being made is not intended to be a criticism. If there is justification for criticism, it might be directed toward any increase in the tendency to attach unwarranted significance to laboratory reports. It is commendable that most laboratories confine their reports to the actual findings. The number of specific tests or examinations is relatively small and the laboratory would therefore rarely be in a position to determine a diagnosis. It should not, of course, be expected to do so.

The physician of former years was compelled by circumstance to rely upon his skill in such basic procedures as observation, palpation, percussion, and auscultation. The conclusions he reached were determined by his own

**Selected Papers of Haven Emerson. Distributed by the American Public Health Association, 1790 Broadway, New York 19, N.Y., for the W. K. Kellogg Foundation, Battle Creek, Michigan. 507 pp. $3.00.*

findings, and he developed judgment through experience. The physician of today may still use the same basic procedures of examination, but he hesitates to draw conclusions until he has in his hands a sheaf of laboratory reports. His problem of assessment has actually increased, for he must determine the significance not only of his own findings on physical examination but also the significance of the findings of the pathologist, bacteriologist, or biochemist.

We need look no further afield than to the serologic test for syphilis to find an obvious example of this state of affairs. The only specific laboratory test for syphilis is the darkfield microscopic examination for *Treponema pallida*, provided that it is performed by a suitably qualified bacteriologist. The serologic test for syphilis is not specific. A positive test report does not necessarily mean that syphilis exists, nor does a negative report necessarily mean that it is absent. These facts are irrefutable and therefore laboratory reports on serologic tests for syphilis must be interpreted by the physician in the light of his clinical findings. The introduction of the quantitative estimates of the reagin content of blood serum may have amplified the available information, but the trend in quantitative titres must also be subjected to interpretation as to its significance. If, therefore, the nomenclature used in serologic test reports is conducive to an assumption that these tests are diagnostic, then appropriate changes are advisable.

There are now few locations on this continent where the practising physician does not have extensive laboratory services within easy access. The majority of physicians have such services so close to hand that they can easily become too convenient. And yet the team composed of the physician and the skilled laboratory technician, co-operating in a relationship of mutual understanding, can make an increasing contribution to the improvement of medical care. If each member of the team applies the full scope of his skill in a manner which is complementary to the other, errors will be at a minimum and decisions will be vindicated by subsequent events.

ABSTRACTS

Aureomycin in Primary Atypical Pneumonia

A GROUP of 22 cases of primary atypical pneumonia treated with aureomycin and a second group of 20 cases of the disease treated with penicillin formed the basis of an evaluation of the two antibiotics in this condition. Definite criteria applied to selection of cases made the two groups highly comparable.

The response to aureomycin was prompt and consistent, the great majority becoming afebrile in three days or less. In the penicillin-treated group approximately one-third of the patients recovered in 48 hours but the majority continued to be febrile for three days or more, and seven of the 20 for more than five days. In addition, four who were seriously ill were switched to aureomycin therapy.

It is of interest that three of the aureomycin-treated group appeared to relapse after the drug was stopped but responded quickly to further doses.

The over-all comparison of the two groups appeared to leave no doubt of the efficacy of aureomycin and the inadequacy of penicillin in the treatment of primary atypical pneumonia.

Gordon Meiklejohn, J.A.M.A., 1949, 140: 891.

The Natural History of the Common Cold

THIS STIMULATING DISCUSSION of the common cold is developed round certain vital questions to which answers were sought by use of human volunteers. While many of the questions remain unanswered, experimental data of value were obtained. Two cold-producing agents were isolated which produced on serial passage in man the clinical picture of the common cold. Takes were obtained in 60 per cent of volunteers. The signs and symptoms were sufficiently constant and regular to regard the condition as an entity. These agents were filtrable, evidently virus in nature, and in size considerably smaller than the influenza virus. Attempts to grow the agents in eggs and to infect other animal species failed.

In only 1 of 19 persons exposed to individuals either in the "pre-symptom" or "full-blown" stages of experimental colds did a frank cold develop. Five others had doubtful symptoms. For this and other reasons it is suggested that colds do not pass readily to "normally resistant" people. Other factors, such as draughts, wet feet and so forth, remain of unknown significance.

The experimental evidence supported the clinical view that colds are especially infectious in the early stages. Washings taken 24 hours before the appearance of symptoms proved to contain virus. Some study was made of the carrier condition and nasal washings from normal persons produced 6 colds in 28 volunteers. Serial transfers to prove that these were virus in nature have yet to be made

While it is recognized that other agents may produce "colds," it is suggested that "It may be useful to consider the possibility that colds are due to a virus which, in a large community, is constantly passing from one person to another, usually causing no symptoms, often only abortive ones, and a real cold only when it finds a victim whose local resistance is for some reason at a temporary low ebb. From such a person it is dispersed in greater quantity. Few people harbour it for long; hence in isolated groups it commonly soon dies out."

The elaborate nature of this project can be gleaned from the introduction in which the conditions, facilities and precautions of the study are described.

C. H. Andrewes, The Lancet, 1949, 6541:71.

Hormone Treatment of the Sexual Offender

THE SUPPRESSION of libido with stilboestrol in two sexually aberrant males and in a number of acromegaly patients treated with oestrone, reported in the literature, suggested this further trial of the method for treatment of sex offenders. In 13 cases, oestradiol or oestrone injections completely abolished libido. Oestradiol in doses of 50,000 I.U. daily gave the desired result within two weeks, and oestrone in similar dosage within four weeks. Continuation of treatment with 20,000 I.U. daily is sufficient to maintain the effect. On intermission of treatment, libido returned within three weeks. Stilboestrol, a cheaper remedy, is apparently effective but slower in action.

The authors feel that the method outlined offers a solution to a difficult problem and is superior to castration, which is mutilating and irregular in results.

F. L. Golla and R. S. Hodge, The Lancet, 1949, 6563:1006.